REMARKS

Applicants acknowledge the current status of the claims, as reported in Office Action dated 6 September 2006. Claims 1-17 are pending; restriction of the claims has been made final and claims 3, 15-17 are withdrawn from consideration; and claims 1-2, and 4-14 are under consideration. Reconsideration and allowance of the application in light of the foregoing amendments and the following remarks are respectfully requested.

Applicants have canceled claims 3, and 15-17. Claims 1and 2 are amended such that the method of treating a skin disorder, and psoriasis, respectively in a subject, comprises administering to the subject a therapeutically effective amount of a neutralizing, high affinity human TNFα antibody, such that said disorder is treated. Claims 4-7 are amended such that they depend only from claims 1or 2. Claims 1, 2, 8, 9, 10 and 13 are amended such that they read upon Applicant's elected species, skin disorder, and within skin disorders, psoriasis. Claim 11 is amended such that the term "or antigen binding fragment thereof" has been deleted. Claim 13 is amended such that the method of treating a subject suffering from the TNFα-related disorder, psoriasis, comprises the step of administering a therapeutically effective amount of D2E7, or an antigen binding fragment thereof, such that said TNFα-related disorder is treated. These amendments are made solely to advance examination of the present application to allowance. These amendments are supported throughout the specification as filed, and no new matter is added. Applicants reserve the right to prosecute the original subject matter in a later-filed continuation application, which properly claims the benefit of this application.

Specification

In the office action at page 3, the Examiner has indicated that the various non-provisional US applications disclosed in the specification should be updated with their current status. Applicants have reviewed the specification and, to the best of Applicants' knowledge, the current status of the various non-provisional US applications disclosed in the specification are up to date. Applicants will continue to update the status of the various applications as necessary. Applicants respectfully request the Examiner to bring to Applicants' attention any non-provisional US applications disclosed in the specification that should be updated.

In the office action at page 4, the Examiner has indicated that the various trademarks disclosed in the specification should be capitalized and should be accompanied by the generic terminology. Applicants have reviewed the specification and, to the best of Applicants' knowledge, the trademarks disclosed in the

specification are capitalized and are accompanied by the generic terminology. Applicants respectfully request the Examiner to bring to Applicants' attention any trademarks that are not capitalized or accompanied by generic terminology.

In the Office Action, at page 4, the Examiner suggests a new title for the present application. Applicants respectfully request consideration of a new title to be held in abeyance, until final disposition and allowance of the claims in the present application.

Claim Objections

In the office action at page 4, the Examiner has objected to claims 1-2 and 4-14 as being drawn to non-elected inventions and has requested appropriate correction. Independent Claims 1, 2, 8, 9, 10 and 13 are amended such that they read upon Applicant's elected species, skin disorder, and within skin disorders, psoriasis. Applicants have canceled claim 3. Claims 4-7 are amended such that they depend only from claims 1 or 2. Thus, claims 1-2 and 4-14, as amended, are drawn to Applicants' elected invention.

In the office action at page 4, the Examiner has objected to claim 11 under 37 CFR 1.75 (c) as being of improper dependent form for failing to further limit the subject matter of a previous claim. Specifically, the Examiner asserts that claim 11, which depends from claim 8, 9 or 10, does not incorporate the CDR3 amino acid substitutions of base claim 9, thus does not further limit the subject matter of previous claim 9. Applicants respectfully disagree.

Applicants have amended claim 11 such that the term "or antigen binding fragment thereof" is deleted. In the method of claim 9, the human antibody, or an antigen-binding fragment thereof has the following characteristics:

a) dissociates from human TNFα with a K_{off} rate constant of 1×10^{-3} s^{-1} or less, as determined by surface plasmon resonance;

b) has a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 3, or modified from SEQ ID NO: 3 by a single alanine substitution at position 1, 4, 5, 7 or 8 or by one to five conservative amino acid substitutions at positions 1, 3, 4, 6, 7, 8 and/or 9;

c) has a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, or modified from SEQ ID NO: 4 by a single alanine substitution at position 2, 3, 4, 5, 6, 8, 9, 10 or 11 or by one to five conservative amino acid substitutions at positions 2, 3, 4, 5, 6, 8, 9, 10, 11 and/or 12.

Therefore, the antibody, or antigen binding fragment, of claim 9 comprises heavy and light chain CDR3 domains of specific amino acid sequence or, comprises heavy and light chain CDR3 domains wherein the specific amino acid sequence has been modified. The antibody in the method of claim 11 (as amended) is D2E7, which is Applicants' most preferred embodiment (see specification page 18, lines 15-19). D2E7 has a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 3, and has a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4. Claim 11 incorporates all the limitations of claim 9 and further limits the antibody to a specific antibody, D2E7. In view of the foregoing, Applicants respectfully request withdrawal of the objection to claim 11 under 37 CFR 1.75 (c) as being of improper dependent form for failing to further limit the subject matter of a previous claim.

Claim rejections under 35 USC §101

In the Office Action, at page 5, claim 13 is rejected under 35 USC §101 because the claim does not set forth any steps involved in the process.

Applicants have amended claim 13 such that the method of treating a subject suffering from the TNFα-related disorder, psoriasis, comprises the step of administering a therapeutically effective amount of D2E7, of an antigen binding fragment thereof, such that said TNFα-related disorder is treated. This amendment is supported throughout the specification as filed, and no new matter is added.

In view of the foregoing amendments and remarks, Applicants respectfully request withdrawal of the rejection of claim 13 under 35 USC §101.

Claim rejections under 35 USC §112 second paragraph

In the Office Action, at page 6, claim 13 is rejected under 35 USC §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as their invention. Specifically, the Examiner asserts that claim does not set forth any steps involved in the process.

Applicants have amended claim 13 such that the method of treating a subject suffering from the TNFα-related disorder, psoriasis, comprises the step of administering a therapeutically effective amount of D2E7, of an antigen binding fragment thereof, such that said TNFα-related disorder is treated. This amendment is supported throughout the specification as filed, and no new matter is added.

In view of the foregoing amendments and remarks, Applicants respectfully request withdrawal of the rejection of claim 13 under 35 USC §112, second paragraph.

Claim rejections under 35 USC §112 first paragraph

In the Office Action, at page 6, claims 7, 11 and 14 are rejected under 35 USC §112 first paragraph, because the specification does not enable one skilled in the art to which it pertains to use the invention. Specifically, the Examiner asserts that the specification does not provide evidence that the claimed biological materials are (1) known and readily available to the public; (2) reproducible from the written description. Applicants respectfully disagree.

Applicants have disclosed, and one of ordinary skill in the art will recognize, that D2E7 is also referred to as HUMIRA® and adalimumab (see specification page 18, lines 15-20). HUMIRA® is well known in the art and readily available to the public. Furthermore, Applicants have provided sufficient guidance with respect to the amino acid sequence of the variable heavy and variable light chains of D2E7. One of ordinary skill in the art can easily make D2E7 using recombinant molecular biological techniques. Contrary to the Examiner's assertion, a deposit of the antibody D2E7, or a cell line that produces the antibody D2E7, is not required for one of ordinary skill in the art to practice Applicants' claimed method.

In view of the foregoing remarks, Applicants respectfully request withdrawal of the rejection of claims 7, 11 and 14, under 35 USC §112, first paragraph.

In the Office Action, at page 10, claims 5, 9 and 12 are rejected under 35 USC §112 first paragraph, as containing subject matter not described in such a way as to enable one skilled in the art to make or use the invention commensurate with the scope of the claim. Specifically the Examiner asserts that the specification only discloses anti-human TNFα antibodies, and antigen binding fragments thereof that comprise all six CDRs, three from heavy chain and three from light chain of D2E7, and the specification does not teach or provide examples of anti-human TNFα antibodies that comprise mutant CDR3 regions of antibody D2E7 and do not comprise the heavy and light chain CDR1 and CDR2 regions from the D2E7 for clinical treatment of anemia related to rheumatoid arthritis. Applicants respectfully disagree.

In the method of claims 5, 9 and 12, the human antibody, or an antigen-binding fragment thereof has to meet the following characteristics:

a) dissociate from human TNFα with a K_{off} rate constant of 1×10^{-3} s^{-1} or less, as determined by surface plasmon resonance;

b) have a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 3, or modified from SEQ ID NO: 3 by a single alanine substitution at position 1, 4, 5, 7 or 8 or by one to five conservative amino acid substitutions at positions 1, 3, 4, 6, 7, 8 and/or 9;

c) have a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, or modified from SEQ ID NO: 4 by a single alanine substitution at position 2, 3, 4, 5, 6, 8, 9, 10 or 11 or by one to five conservative amino acid substitutions at positions 2, 3, 4, 5, 6, 8, 9, 10, 11 and/or 12.

The Examiner cites Paul, Fundamental Immunology, 3rd Edition, 1993, pp.292-295; and asserts that the formation of an intact antigen-binding site of antibodies requires the association of the complete heavy and light chain variable regions of a given antibody, each of which consist of three CDRs, and provide the majority of the contact residues for the binding of the antibody to its target epitope. Applicants respectfully submit that the state of the art in recombinant antibody technology has changed significantly since 1993. Applicants assert the fact that not all of the CDRs of the antigen binding site may be necessary (or even utilized) in binding a specific antigen, and that functional antibody fragments comprising fewer than all 6 CDRs is well known by practitioners skilled in the art. In the specification as filed, on pages 7-8, Applicants teach and disclose examples of binding fragments encompassed within the term "antigen-binding portion" of an antibody include (i) a Fab fragment, a monovalent fragment consisting of the VL, VH, CL and CH1 domains; (ii) a F(ab')2 fragment, a bivalent fragment comprising two Fab fragments linked by a disulfide bridge at the hinge region; (iii) a Fd fragment consisting of the VH and CH1 domains; (iv) a Fv fragment consisting of the VL and VH domains of a single arm of an antibody, (v) a dAb fragment (Ward et al., (1989) Nature 341:544-546), which consists of a VH domain; and (vi) an isolated complementarity determining region (CDR). Not withstanding the foregoing, no matter how many CDRs the binding fragment contains, the antibody or antigen binding fragment must dissociate from human TNFα with a K_{off} rate constant of 1×10^{-3} s^{-1} or less, as determined by surface plasmon resonance.

The Examiner cites Rudikoff et al (Proc. Natl. Acad. Sci. USA, 79(6):1979-1983, March 1982) and asserts that even minor changes in the amino acid sequence of the heavy and light chain variable regions may dramatically affect antigen binding function. The Examiner further asserts that the applicants have not provided sufficient guidance in the specification, there are no working examples, and undue experimentation would be required to practice the claimed therapeutic method. Applicants respectfully disagree.

The MPEP §2164.06 in relevant part provides that:

> The quantity of experimentation needed to be performed by one skilled in the art is only one factor involved in determining whether "undue experimentation" is required to make and use the invention. "[A]n extended period of experimentation may not

> be undue if the skilled artisan is given sufficient direction or guidance." In re Colianni, 561 F.2d 220, 224, 195 USPQ 150, 153 (CCPA 1977). " 'The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.' " In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (citing In re Angstadt, 537 F.2d 489, 502-04, 190 USPQ 214, 217-19 (CCPA 1976)). Time and expense are merely factors in this consideration and are not the controlling factors. United States v. Telectronics Inc., 857 F.2d 778, 785, 8 USPQ2d 1217, 1223 (Fed. Cir. 1988), cert. denied, 490 U.S. 1046 (1989).

It is also recognized that:

> The presence of inoperative embodiments within the scope of a claim does not necessarily render a claim nonenabled. The standard is whether a skilled person could determine which embodiments that were conceived, but not yet made, would be inoperative or operative with expenditure of no more effort than is normally required in the art. Atlas Powder Co. v. E.I. du Pont de Nemours & Co., 750 F.2d 1569, 1577, 224 USPQ 409, 414 (Fed. Cir. 1984) (prophetic examples do not make the disclosure nonenabling).
>
> MPEP §2164.08(b)

As stated above, the antibody or antigen binding fragment of methods of claim 5, 9 and 12 must not only have specific heavy and light chain CDR 3 sequences, but must also dissociate from human TNFα with a K_{off} rate constant of 1×10^{-3} s^{-1} or less, as determined by surface plasmon resonance.

Applicants submit that the teachings of the specification and the knowledge in the art are commensurate with the scope of the claims, and one of ordinary skill in the art would not have to perform undue experimentation to perform the methods of the invention. The specification teaches at page 18-20, that heavy and light chain CDR3 domains play an important role in the binding specificity/ affinity of an antibody for an antigen and that the CDR3 domains of the light and heavy chain sequences of the antibody D2E7, *i.e.,* those CDRs recited in the claim, have advantageous properties for use in the invention. The specification describes not only the sequences of the light and heavy chain CDR3 domains, but also various substitutions which may be made within the CDR3 domains such that the CDR3 domain retains its high affinity binding characteristic. The instant specification also references U.S. Patent No. 6,090,382 (see, for example, page 18, lines 19-20) which characterizes the CDR3 domains of SEQ ID NOs: 3 and 4.

In contrast to the Examiner's assertion, one of ordinary skill in the art would know how to make the antibodies, and antigen-binding portions thereof, described in the claims. The specification describes methods for making and expressing antibodies, and antigen-binding portions thereof, for use in the methods of the invention particularly at pages 24-31. In addition, methods for making and expressing antibodies and antigen-binding portions thereof used in the invention were known in the art. Thus, in view of the fact that the CDR3 sequences described in claim 5, 9 and 12, are described in the specification and known in the art as having high affinity for human TNFα, and that one of ordinary skill in the art would know how to make antibodies, or antigen-binding portions thereof, commensurate with the claims. In addition, as stated above the quantity of experiments is not determinative for 'undue experimentation'. One of ordinary skill in the art will recognize that the amount of experimentation needed is routine and by no means undue. Thus, Applicants' disclosure, in combination with the state of the art at the time of the invention, enables one of skill in the art to perform the methods of the claimed invention without undue experimentation.

In view of the foregoing amendments and remarks, Applicants respectfully request withdrawal of the rejection of claims 5, 9 and 12, under 35 USC §112, first paragraph.

Claim rejections under 35 USC §102

In the Office Action, at page 14, the Examiner has rejected claims 1-2, and 13 under 35 USC §102(b) as being anticipated by Oh et al (Journal of American Academy of Dermatology, 42(5):829-830, 2000). The Examiner asserts that Oh et al., teach a method of treating psoriasis by administering a therapeutically effective amount of a neutralizing, high affinity TNFα antibody such that psoriasis is treated and thus anticipates Applicants' claimed invention. Applicants respectfully disagree.

35 U.S.C. §102, in relevant part, states that:

> A person shall be entitled to a patent unless –
>
> > (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Applicants' invention as amended, is directed to a method of treating a skin disorder, and psoriasis, respectively in a patient by administering a therapeutically effective amount of a neutralizing, high affinity human TNFα antibody, such that the disorder is treated.

Oh et al., disclose a method of psoriasis by administering a therapeutically effective amount of a chimeric anti- TNFα antibody, Infliximab. Oh et al., do not teach or suggest a method of treating a skin disorder, or psoriasis, in a patient by administering a therapeutically effective amount of a neutralizing, high affinity human TNFα antibody, such that the disorder is treated.

Oh et al., do not teach or suggest each and every element of the present invention either expressly or inherently; i.e., method of treating skin disorder or psoriasis in a patient by administering a therapeutically effective amount of a neutralizing, high affinity human TNFα antibody, such that the disorder is treated. Because the cited reference does not teach or suggest the claimed methods of the invention, it fails to anticipate Applicants' invention.

In view of the foregoing remarks, Applicants submit the present invention as claimed is patentable over Oh et al. Applicants therefore respectfully request withdrawal of the rejection of claims 1-2 and 13 under 35 USC §102(b).

In the Office Action, at page 15, the Examiner has rejected claims 1-2, and 13 under 35 USC §102(b) as being anticipated by Ogilvie et al (British Journal of Dermatology, 144(3):587-589, March 2001). The Examiner asserts that Ogilvie et al., teach a method of treating psoriasis by administering a therapeutically effective amount of a neutralizing, high affinity TNFα antibody such that psoriasis is treated and thus anticipates Applicants' claimed invention. Applicants respectfully disagree.

As stated above, Applicants' invention as amended, is directed to a method of treating a skin disorder, and psoriasis, respectively in a patient by administering a therapeutically effective amount of a neutralizing, high affinity human TNFα antibody, such that the disorder is treated.

Ogilvie et al., disclose a method of psoriasis by administering a therapeutically effective amount of a chimeric anti- TNFα antibody, Infliximab. Ogilvie et al., do not teach or suggest a method of treating a skin disorder, or psoriasis, in a patient by administering a therapeutically effective amount of a neutralizing, high affinity human TNFα antibody, such that the disorder is treated.

Ogilvie et al., do not teach or suggest each and every element of the present invention either expressly or inherently; i.e., method of treating skin disorder or psoriasis in a patient by administering a therapeutically effective amount of a neutralizing, high affinity human TNFα antibody, such that the disorder is treated. Because the cited reference does not teach or suggest the claimed methods of the invention, it fails to anticipate Applicants' invention.

In view of the foregoing remarks, Applicants submit the present invention as claimed is patentable over Ogilvie et al. Applicants therefore respectfully request withdrawal of the rejection of claims 1-2 and 13 under 35 USC §102(a).

Rejections under 35 USC §103(a)

In the Office Action, at page 16, claims 1-2 and 4-14 are rejected under 35 USC §103(a) as being unpatentable over Oh et al (Journal of American Academy of Dermatology, 42(5):829-830, 2000) in view of Salfeld et al. (WO 97/29131, publication date 8/14/1997). The Examiner asserts that it would be obvious to one skilled in the art to combine the teachings of Oh et al., with those of Salfeld et al to arrive at Applicants' invention directed to a method of treating Skin disorders, and in particular psoriasis in a patient by administering a therapeutically effective amount of a neutralizing, high affinity human TNFα antibody, such that the disorder is treated. Applicants respectfully disagree.

BASIC REQUIREMENTS OF A *PRIMA FACIE* CASE OF OBVIOUSNESS

> To establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all claim limitations.
>
> MPEP §2143

As amended, Applicant's claimed invention is directed to a method of treating a skin disorder, and psoriasis, respectively in a patient by administering a therapeutically effective amount of a neutralizing, high affinity human TNFα antibody, such that the disorder is treated. Claims 4-14 recite specific aspects of Applicant's invention.

Oh et al., disclose a method of treating psoriasis by administering a therapeutically effective amount of a chimeric anti- TNFα antibody, Infliximab. Oh et al., do not teach or suggest a method of treating a skin disorder, and psoriasis, respectively in a patient by administering a therapeutically effective amount of a neutralizing, high affinity human TNFα antibody, such that the disorder is treated.

Salfeld et al (WO 97/29131) disclose a method of treating a patient with rheumatoid arthritis with human anti-TNFα antibodies. Salfeld et al (WO 97/29131) do not teach or suggest a method of treating a skin disorder, and psoriasis, respectively in a patient by administering a therapeutically effective amount of a neutralizing, high affinity human TNFα antibody, such that the disorder is treated. The Examiner asserts that one of ordinary skill in the art would have been reasonably expected to combine the teaching of Oh et al., with those of Salfeld et al (WO 97/29131) to arrive at Applicants' invention, i.e. method of treating a skin disorder, and psoriasis, respectively in a patient by administering

a therapeutically effective amount of a neutralizing, high affinity human TNFα antibody, such that the disorder is treated. Neither Oh et al., nor Salfeld et al (WO 97/29131), either singularly or in combination, teach or suggest a method of treating a skin disorder, and psoriasis, respectively in a patient by administering a therapeutically effective amount of a neutralizing, high affinity human TNFα antibody, such that the disorder is treated.

Applicants assert there is no suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the references or to combine the reference teachings (required as the first criterion to establish a *prima facie* case of obviousness) to arrive at a method of treating a skin disorder, and psoriasis, respectively in a patient by administering a therapeutically effective amount of a neutralizing, high affinity human TNFα antibody, such that the disorder is treated. In addition, the references either singularly, or in combination, do not teach or suggest all claim limitations, i.e. treat skin disorder, and in particular psoriasis in a patient by administering a therapeutically effective amount of a neutralizing, high affinity human TNFα antibody.

Because the cited art fails to satisfy the criteria necessary to establish or to sustain rejection of claims 1-2 and 4-14 as obvious under 35 USC §103(a), and in view of the foregoing remarks, Applicants respectfully request withdrawal of the rejection of claims 1-2 and 4-14 under 35 USC §103(a).

In the Office Action, at page 21, claims 1-2 and 4-14 are rejected under 35 USC §103(a) as being unpatentable over Oh et al (Journal of American Academy of Dermatology, 42(5):829-830, 2000) in view of Salfeld et al. (US Patent 6,509,015 B1, 2/9/1996). The Examiner asserts that it would be obvious to one skilled in the art to combine the teachings of Oh et al., with those of Salfeld et al to arrive at Applicants' invention directed to a method of treating Skin disorders, and in particular psoriasis in a patient by administering a therapeutically effective amount of a neutralizing, high affinity human TNFα antibody, such that the disorder is treated. Applicants respectfully disagree.

As amended, Applicant's claimed invention is directed to a method of treating a skin disorder, and psoriasis, respectively in a patient by administering a therapeutically effective amount of a neutralizing, high affinity human TNFα antibody, such that the disorder is treated. Claims 4-14 recite specific aspects of Applicant's invention.

Oh et al., disclose a method of treating psoriasis by administering a therapeutically effective amount of a chimeric anti- TNFα antibody, Infliximab. Oh et al., do not teach or suggest a method of treating a skin disorder, and psoriasis, respectively in a patient by administering a therapeutically effective amount of a neutralizing, high affinity human TNFα antibody, such that the disorder is treated.

Salfeld et al (US Patent 6,509,015 B1) disclose a method of treating a patient with rheumatoid arthritis with human anti-TNFα antibodies. Salfeld et al (US Patent 6,509,015 B1) do not teach or

suggest a method of treating a skin disorder, and psoriasis, respectively in a patient by administering a therapeutically effective amount of a neutralizing, high affinity human TNFα antibody, such that the disorder is treated. The Examiner asserts that one of ordinary skill in the art would have been reasonably expected to combine the teaching of Oh et al., with those of Salfeld et al (US Patent 6,509,015 B1) to arrive at Applicants' invention, i.e. method of treating a skin disorder, and psoriasis, respectively in a patient by administering a therapeutically effective amount of a neutralizing, high affinity human TNFα antibody, such that the disorder is treated. Neither Oh et al., nor Salfeld et al (US Patent 6,509,015 B1), either singularly or in combination, teach or suggest a method of treating a skin disorder, and psoriasis, respectively in a patient by administering a therapeutically effective amount of a neutralizing, high affinity human TNFα antibody, such that the disorder is treated.

Applicants assert there is no suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the references or to combine the reference teachings (required as the first criterion to establish a *prima facie* case of obviousness) to arrive at a method of treating a skin disorder, and psoriasis, respectively in a patient by administering a therapeutically effective amount of a neutralizing, high affinity human TNFα antibody, such that the disorder is treated. In addition, the references either singularly, or in combination, do not teach or suggest all claim limitations, i.e. treat skin disorder, and in particular psoriasis in a patient by administering a therapeutically effective amount of a neutralizing, high affinity human TNFα antibody.

Because the cited art fails to satisfy the criteria necessary to establish or to sustain rejection of claims 1-2 and 4-14 as obvious under 35 USC §103(a), and in view of the foregoing remarks, Applicants respectfully request withdrawal of the rejection of claims 1-2 and 4-14 under 35 USC §103(a).

Double Patenting

Obviousness type double patenting

In the Office Action, at page 26, claims 1-2 and 4-14 are rejected under the judicially created doctrine of obviousness double patenting as being unpatentable over claims 1-7, 16, 36-39, 48 and 69-70 of U.S. Patent No. 6,509,015 B1 in view of Oh et al., (Journal of American Academy of Dermatology, 42(5):829-830, 2000). Applicants respectfully disagree.

U.S. Patent No. 6,509,015 B1 discloses a method of treating a patient with rheumatoid arthritis with human anti-TNFα antibodies. U.S. Patent No. 6,509,015 B1 does not teach or suggest a method of treating a skin disorder, and psoriasis, respectively in a patient by administering a therapeutically effective amount of a neutralizing, high affinity human TNFα antibody, such that the disorder is treated.

As stated above, Oh et al., disclose a method of treating psoriasis by administering a therapeutically effective amount of a chimeric anti- TNFα antibody, Infliximab. Oh et al., do not teach or suggest a method of treating a skin disorder, and psoriasis, respectively in a patient by administering a therapeutically effective amount of a neutralizing, high affinity human TNFα antibody, such that the disorder is treated.

Applicants respectfully submit that the cited reference does not teach or suggest the claimed methods of the invention. Therefore, claims 1-2 and 4-14 are not obvious in view of the cited art. Accordingly, the rejection of claims 1-2 and 4-14 under the judicially created doctrine of obviousness double patenting as being unpatentable over claims 1-7, 16, 36-39, 48 and 69-70 of U.S. Patent No. 6,509,015 B1 in view of Oh et al., (Journal of American Academy of Dermatology, 42(5):829-830, 2000) should be withdrawn.

In the Office Action, at page 28, claims 1-2 and 4-14 are provisionally rejected under the judicially created doctrine of obviousness double patenting as being unpatentable over claims 1-23, and 73-84 of co-pending U.S. Application No. 10/163,657 in view of Oh et al., (Journal of American Academy of Dermatology, 42(5):829-830, 2000). Applicants respectfully disagree.

Co-pending U.S. Application No. 10/163,657 claims a method of treating a patient with rheumatoid arthritis with a bi-weekly dose of human anti-TNFα antibodies. Co-pending U.S. Application 10/163,657 does not teach or suggest a method of treating a skin disorder, and psoriasis, respectively in a patient by administering a therapeutically effective amount of a neutralizing, high affinity human TNFα antibody, such that the disorder is treated.

As stated above, Oh et al., disclose a method of treating psoriasis by administering a therapeutically effective amount of a chimeric anti- TNFα antibody, Infliximab. Oh et al., do not teach or suggest a method of treating a skin disorder, and psoriasis, respectively in a patient by administering a therapeutically effective amount of a neutralizing, high affinity human TNFα antibody, such that the disorder is treated.

For reasons stated above, claims 1, 2 and 4-14 are not obvious in view of the cited art. Accordingly, the rejection of claims 1-2 and 4-14 under the judicially created doctrine of obviousness double patenting as being unpatentable over claims 1-23, and 73-84 of co-pending U.S. Application No. 10/163,657 in view of Oh et al., (Journal of American Academy of Dermatology, 42(5):829-830, 2000) should be withdrawn.

In the Office Action, at page 31, claims 1-2 and 4-14 are provisionally rejected under the judicially created doctrine of obviousness double patenting as being unpatentable over claim 15 of co-

pending U.S. Application No. 11/233,252 in view of Oh et al., (Journal of American Academy of Dermatology, 42(5):829-830, 2000) and Salfeld et al (WO 97/29131). Applicants respectfully disagree.

Co-pending U.S. Application 11/233,252 claims a method of treating a patient with rheumatoid arthritis and other diseases, but not a skin disorder, and psoriasis, with anti-TNFα antibodies. Co-pending U.S. Application 11/233,252 does not teach or suggest a method of treating a skin disorder, and in particular psoriasis, in a patient by administering a therapeutically effective amount of a neutralizing, high affinity human TNFα antibody, such that the disorder is treated

For reasons stated above, Oh et al., and Salfeld et al (WO 97/29131) do not teach or suggest Applicants' claimed method either singularly or in combination. Accordingly, the rejection of claims 1-2 and 4-14 under the judicially created doctrine of obviousness double patenting as being unpatentable over claim 15 of co-pending U.S. Application No. 11/233,252 in view of Oh et al., (Journal of American Academy of Dermatology, 42(5):829-830, 2000) and Salfeld et al (WO 97/29131), should be withdrawn.

In the Office Action, at page 34, claims 1-2 and 4-14 are rejected provisionally under the judicially created doctrine of obviousness double patenting as being unpatentable over claims 1-5 and 7-26 and 28-53 of co-pending U.S. Application No. 11/104,117 in view of Oh et al., (Journal of American Academy of Dermatology, 42(5):829-830, 2000). Applicants respectfully disagree.

Co-pending U.S. Application No. 11/104,117 claims a multiple-variable dose of TNFα inhibitor for treating a disorder, including skin disorder and psoriasis, in which TNFα activity is detrimental. For reasons stated above, Oh et al., do not teach or suggest a method of treating a patient with skin disorder, in particular psoriasis, by administering a therapeutically effective amount of a neutralizing, high affinity human TNFα antibody, such that the disorder is treated.

Applicants request the Examiner to hold this rejection with respect to co-pending U.S. Application No. 11/104,117 in abeyance until final disposition and allowance or claims in the instant application.

In the Office Action, at page 38, claims 1-2 and 4-14 are rejected provisionally under the judicially created doctrine of obviousness double patenting as being unpatentable over claims 1-10 and 14-27 of co-pending U.S. Applications 10/622,205.

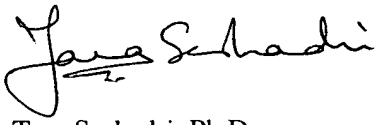
Upon determination of allowable subject matter in the instant application, Applicants will cancel claims directed to method of treating a skin disorder, in particular psoriasis, with TNF-α inhibitor from co-pending US application 10/622,205.

In view of the foregoing remarks, Applicants respectfully request withdrawal of the rejection of claims 1-2 and 4-14 under the judicially created doctrine of obviousness double patenting.

Conclusion

In view of the foregoing amendments and remarks, Applicants believe the rejections set forth in the Office Action dated 6 September 2006 have been avoided or overcome, and consequently their application is in condition for allowance. Applicants, therefore, respectfully request reconsideration and withdrawal of the rejections, and allowance of the pending claims as amended.

Respectfully submitted,



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